Milano, May 19,1953

Dear Joshua,enclosed is the final draft of the joint paper,to be
published on Chain's symposium. When your comments came I rewrote
the paper taking your suggestions into account,and resisting as much
as I could the temptation of altering the text while polishing it up.
Jinks read the whole thing and suggested a number of alterations of
the place for prepositions and conjunctions -of course,in my own
part. You probably overrate my capacity for writing English . The
only paper which was written entirely by myself is the one on Here-
dity,chloramphenicoll-resistance;/the W.H.O. paper ~~owes~~ I owe much
to the kindness of Dr.Ercoli,formerly director of this Istituto and
now working at Armour's.Unfortunately ,due to a mistake,his help in
the correction of the manuscript was not acknowledged in the paper.

I hope you will find the present work tolerably good.However,
there is a chance to improve it,since Chain,to whom I explained on
Monday last that you had not seen the final version,promised to send
me proofs. I do not know when proofs will actually come,so it would
be best if you could send me a copy of the manuscript with your cor-
rections ~~if~~ as soon as you can manage. Two copies enclosed so that
you can keep one.

The first part was altered more than the rest,in order ~~to~~ follow
your suggestions . I dropped Law's quotation (Texas Reports Biol.&
Med. 10:571) because it is not quite clear whether his test is a fluc-
tuation test or a correlation between relatives test;it is probably
a mixture of the two,since weight of tumor/depends should both on absolute
number of resistant cells (fluctuation test) and growth rate of indi-
vidual mutations(correl.betw.rel.). Some bibliog.references may be
incomplete (e.g., Catlin's). As to the negative binomial story,I have
kept it (but am ready to drop it in proofs). I think the variance of
numbers of resistants ~~would~~ in parallel cultures would ~~have a variance~~
be definitely greater than the mean if the probability of becoming
resistant were ~~higher~~ variable from cell to cell(proportional to
cell size,for instance,to give an unlikely physiological example).
However,I am not a mathematician [perhaps because of this reason
I fully agree with you as to the poor persuading power of indirect mathe-
matical proofs,including kinetics; although ,in the end,all proofs
may be put in biometrical terms,~~except that~~ the kinds of proofs of
which replica plating is a splendid example need not be put in bio-
metrical terms to be convincing,and derive part of their strength
from this fact] and cannot consult anybody here on the issue,but you
may in Madison. The same kind of argument for deriving say, ~~abinomial~~
a negative binomial,~~for~~ has been employed by Greenwood and Yule to
explain the non-poissonian distribution of deaths by accidents in in-

dustry. They assumed a variable degree of accident proneness
in the population;and if this degree were variable according to
a distribution of chi square type (Eulerian or Pearson type III)
the observed distribution of number of deaths per year should
be the negative binomial,which in fact they found. Of course,the
extra parameter permits a wide adjustability and the hypothesis
has no biological interest.It serves to stress that ,when testing
for mutation and selection versus physiological adaptation,the
latter cannot be denied by the simple assumption of a Poisson
distribution ,and the finding that this will not fit. Therefore
I believe the fluctuation test is not test at all. I have kept
its original designation to avoid the introduction of further
nomenclature.
I hope you will take a free hand in the discussion of the manu-
script. As to reprints I have noted your wishes.
Work : Calef,working here, has crossed coli B to K-12;the fre-
quency of recombination is low,but higher with Hfr. (Demerec will
now be unexcusable if he does not carry out genetic ana-
lyses of his mutants). The interesting thing is that cros-
sing a Tr-coli B to Hfr $S^r$ on minimal sm tryptophane,the Tr- $S^r$
recombinants are all Hfr ! Both when crossed to K-12 F- and to
coli B. Coli B behaves as F- and when crossed to K-12 F+ gives
F- progeny;it cannot be infected. These results are highly preli-
minary and I hope they will stand further trials.
I have been quite convinced by your idea of a book on Genetics
and Chemotherapy. Would there be a chance of writing it jointly
if I could come to the USA for a period?
Perhaps next summer may-be (1954) will be my first opportunity
for trying to get a leave. I am bound here both by routine and by
academic duties,and summer is unfortunately the best time.If you
spend at least part of it in Madison,I might see in the meanwhile
a few other places of interest,while you are away.June-October is
the longest stretch of time I can think of ,in view of my present
duties. You wrote some time ago that there may be a chance of get-
ting local funds for my living expenses;it would be easier if I
had to get money only for the journey,or little more. I should li-
ke to come with my wife to give me a help in the lab and in the
library,but would leave the rest of the family home. If you let
me know your opinion,and I can confirm the prospects of a leave,
I shall apply to the Rockefeller first,and then perhaps W.H.O.
Yours

Luca